New Concept: Testing Centers for Development of Somatic Cell Genome Editing in Model Organisms

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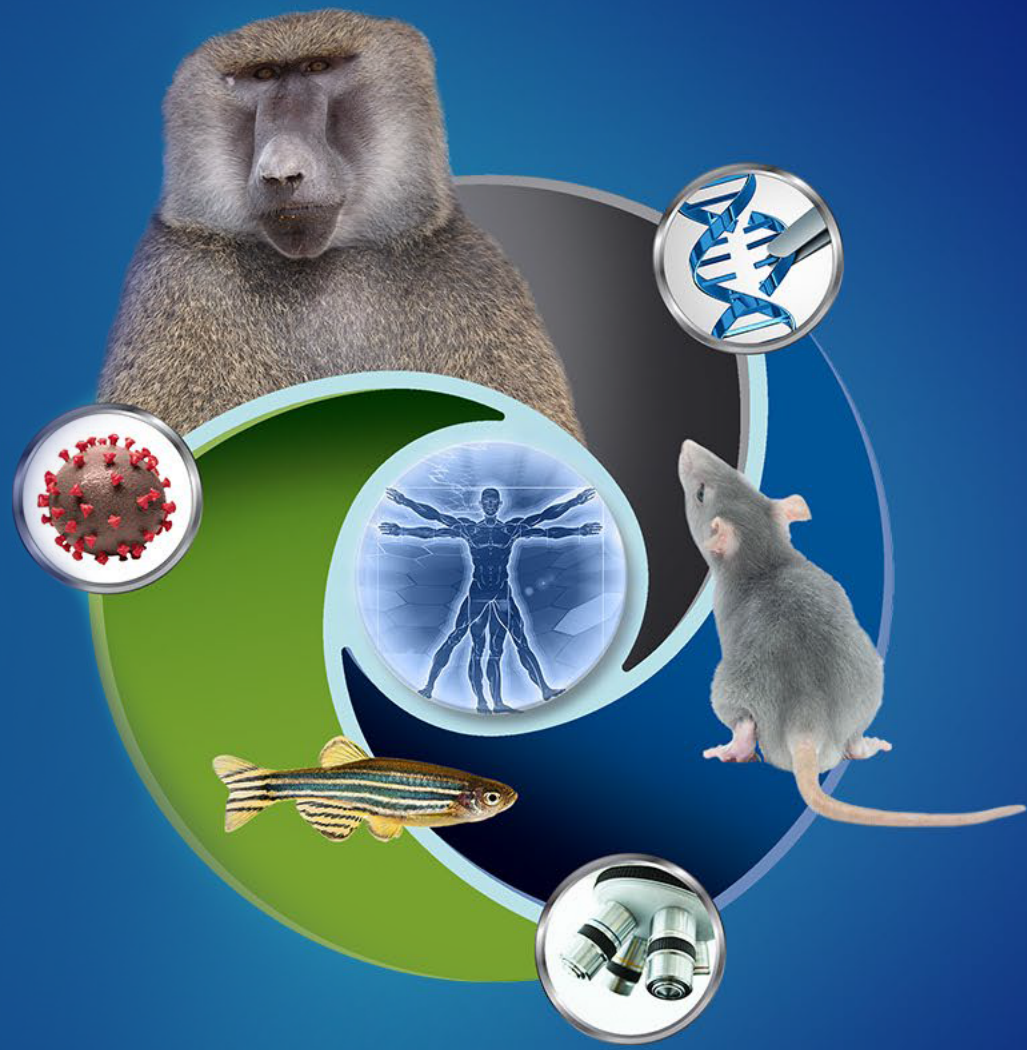

ORIP
OFFICE OF RESEARCH INFRASTRUCTURE PROGRAMS

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Concept Clearance: New

Testing Centers for Development of Somatic Cell Genome Editing in Model Organisms

Objective: To support Testing Centers aimed at providing broadly applicable resources and testing services in reporter animals and disease models for investigators developing somatic cell genome editing (SCGE) therapeutics relevant to the interests of multiple NIH Institutes, Centers, and Offices (ICOs)

Funds Available and Anticipated Number of Awards:

- Contingent upon NIH appropriations and submission of highly meritorious applications
- Expectation is to fund at least one Testing Center for the following mammalian model animal species: rodents (e.g., mice, rats), pigs, and nonhuman primates (NHPs)

Award Project Period: 5 years

Council Action: Vote for approval of the concept for "Testing Centers for Development of Somatic Cell Genome Editing in Model Organisms."

Background

Impact of *in vivo* Genome Editing

- CRISPR-Cas9 catalyzed the development of experimental genome editing therapeutics, with the first-in-human trial in 2021.
- Genome editing allows precise corrections to be made in patients' DNA and RNA.
- Thousands of genetic diseases are amenable to targeted *in vivo* genome editing approaches.

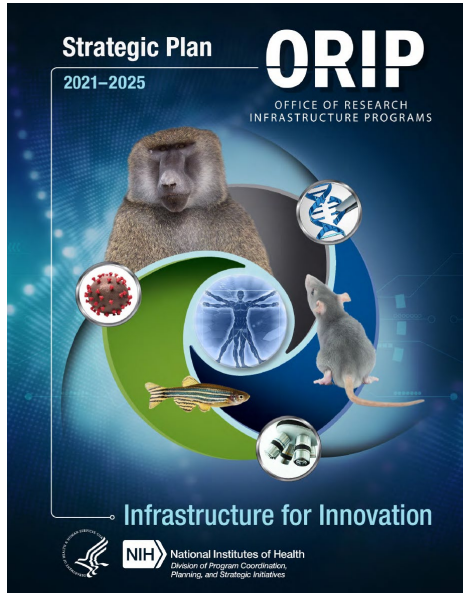
Well-Documented Need for Testing SCGE in Animal Models

- Gaps and opportunities from Common Fund Planning Workshop (2017; NIH)
- Somatic Cell Genome Editing Program Phase II Planning Workshop (2021; NIH)
- Prenatal Somatic Cell Gene Therapies: Charting a Path Forward for Clinical Applications (2021; University of California, San Francisco/U.S. Food and Drug Administration [FDA])
- New guidance on Human Gene Therapy Products Incorporating Human Genome Editing (2022; FDA-2021-D-0398)

Background

ORIP Strategic Plan 2021–2025

- Facilitate the development and ensure the availability of the highest quality and most useful animal models and related resources for the advancement of research on human disease.
- Improve and disseminate the best models for human conditions and diseases that are of interest to multiple NIH Institutes and Centers (ICs).
- Advance the application of new technologies to support research resources and improve the generation, care, preservation, and distribution of animal models.



https://orip.nih.gov/sites/default/files/ORIP_Strategic_Plan_2021-2025_508.pdf

Background

Current SCGE Efforts

- As part of its SCGE Program, the NIH Common Fund supports testing new delivery and genome editing technologies in healthy animals and creation of reporter animals through small-animal (e.g., rodents) and large-animal (e.g., pigs, NHPs) Testing Centers.
    - These Centers and large-animal reporter generation projects are administered by ORIP.
    - Testing of new delivery technologies under disease conditions is not being addressed at this time.
    - Accessibility to the wider research community will be needed.
- SCGE Program has produced several validated rodent reporter models, with creation and preliminary validation of larger reporter animals, especially NHPs, being planned toward the end of this Program.
    - In-depth validation of reporter models, creation of animal cohorts, and availability to investigators will require additional support and special expertise.
    - Coordination of services to use these models will be needed.

Proposed New Initiative

To align with ORIP's NIH-wide mission, the proposed Testing Centers should:

- Have the ability to use wild-type and reporter animals, as well as disease models, relevant to the interest of multiple NIH ICOs.
- Have the capacity and expertise to evaluate genome editing across a variety of disease conditions.
- Offer resources and services to the wider biomedical community that have a significant impact on rigor and reproducibility of animal studies.
- Provide animal resources and services to assist in development of new technologies and preclinical testing to generate high-quality, reproducible information required for clinical studies.
- Coordinate their activities with the SCGE Program, as well as other programs at NIH ICOs, such as the Bespoke Gene Therapy Consortium and the Ultra-Rare Gene-based Therapy (URGenT) Network (National Institute of Neurological Disorders and Stroke).
- Develop outreach and advertisements for the program to solicit requests for fee-for-service use and collaborative studies.

Purpose of New Initiative

The initiative will support resources and services for testing SCGE not only in healthy animals but also in animal models for human disease for the wider biomedical community.

Proof-of-concept studies using prenatal gene editing in large-animal species (e.g., swine, NHPs) for the treatment of inherited genetic diseases will be a high priority.

Concept Clearance

Vote for approval of the concept for "Testing Centers for Development of Somatic Cell Genome Editing in Model Organisms."